

Applicant(s) : Guangwen WEI, et al.
U.S. Serial No.: 10/650,365
Filed : August 28, 2003
Page : 2

Amendments to the Specification:

Page 1, line 25:

IFN-con~~IFN- α~~ is a new interferon molecule constructed with the

Page 1, line 29:

it. IFN-con~~IFN- α~~ had been proved to have broad-spectrum IFN

Page 1, line 32:

Inc. addresses treatment IFN-con~~IFN- α~~ . Chinese Patent No.

Page 1, line 33-34:

97193506.8 by Amgen, Inc. addresses re-treatment of ~~IFN- α~~
consensus interferon on hepatitis C. Chinese Patent No.
98114663.5 by

Page 1, line 35-36:

Shenzhen Jiusheng Bio-engineering Ltd. addresses ~~treatment of~~
~~IFN- α~~ recombinant human consensus interferon- α treatment on
for hepatitis B and hepatitis C.

Page 2, line 1:

authorized Amgen to produce ~~IFN- α~~ INFERGEN® (interferon
alfacon-1) with *E. Coli*. for

Applicant(s) : Guangwen WEI, et al.
U.S. Serial No.: 10/650,365
Filed : August 28, 2003
Page : 3

BEST AVAILABLE COPY

Page 4, lines 4 and 5:

Figure 1. rSIFN-co cDNA sequence (~~Seq. ID No.~~ SEQ ID NO:1)
designed according to E. Coli. codon usage and deduced rSIFN-
co amino acid sequence (~~Seq. ID No.~~ SEQ ID NO:2)

Page 4, line 7:

Figure 2. Sequence of another super-compound interferon (~~Seq. ID Nos.~~ SEQ ID NOS: 3&4)

Page 4, line 15:

Figure 6-A. Circular Dichroism spectrum of ~~Interferon~~ INFERGEN[®]
(interferon alfacon-1)

On page 4, please delete the paragraph beginning at line 23
and insert the following paragraph in its place:

INFERGEN[®] (interferon alfacon-1), made by Amgen Inc., also
known as consensus interferon, is marketed for the treatment
of adults with chronic hepatitis C virus (HCV) infections. It
is currently the only FDA approved, bio-optimized interferon
developed through rational drug design and the only interferon
with data in the label specifically for non-responding or
refractory patients. InterMune's sales force re-launched
INFERGEN[®] (interferon alfacon-1) in January 2002 with an active
campaign to educate U.S. hepatologists about the safe and
appropriate use of INFERGEN[®] (interferon alfacon-1), which
represents new hope for the more than 50 percent of HCV
patients who fail other currently available therapies.

Page 5, line 1:

Figure 6-B. Circular Dichroism spectrum of ~~Interferon~~ INFERGEN[®]
(interferon alfacon-1) From Reference [Journal of Interferon
and Cytokine Research. 16:489-499(1996)]

Page 5, line 22:

Applicant(s) : Guangwen WEI, et al.
U.S. Serial No.: 10/650,365
Filed : August 28, 2003
Page : 4

Clearly, as evidenced by the above spectra, the secondary or even tertiary structure of rSIFN-co is different from ~~Infergen~~INFERGEN[®] (interferon alfacon-1).

Page 14, line 24:

Oligomer A (~~Seq. ID No.~~SEQ ID NO:5):

Page 14, line 27:

Oligomer B (~~Seq. ID No.~~SEQ ID NO:7):

Page 14, line 30:

Oligomer C (~~Seq. ID No.~~SEQ ID NO:8):

Page 14, line 33:

Oligomer D (~~Seq. ID No.~~SEQ ID NO:9):

Page 15, line 2:

Oligomer E (~~Seq. ID No.~~SEQ ID NO:10):

Page 15, line 5:

Oligomer F (~~Seq. ID No.~~SEQ ID NO:11):

Page 16, line 11:

Oligomer G (~~Seq. ID No.~~SEQ ID NO:12):

5'ATCGGCCATATGTGCGACCTGCCGCAGACCC3'

Page 16, line 12:

Oligomer H (~~Seq. ID No.~~SEQ ID NO:13):

5'ACTGCCAGGCTGCAGTTATTCTTTACGACGCAGACGTTCC3'

Page 17, line 19:

(SEQ ID NO: 14) N- Cys-Asp-Leu-Pro-Gln-Thr-His-Ser-Leu-Gly-
Asn-Arg-Arg-Ala-Leu-

Applicant(s) : Guangwen WEI, et al.
U.S. Serial No.: 10/650,365
Filed : August 28, 2003
Page : 5

Page 20, line 22

rSIFN-co CDNA SEQUENCE (SEQ ID NO:1) DESIGNED ACCORDING TO E.
COLI. CODON USAGE AND DEDUCED rSIFN-co AMINO ACID SEQUENCE_
(SEQ ID NO:2)

On page 29, please delete the paragraph beginning at line 7 and insert the following paragraph in its place:

Control drugs: IFN- α 2b (Intron A) as lyophilized powder, purchased from Schering Plough. 3×10^6 U each, mix to 3×10^6 IU/ml with culture medium; INFERGEN[®] (interferon alfacon-1) (liquid solution) , purchased from Amgen, 9 μ g, 0.3ml each, equal to 9×10^6 IU, and mix with 9×10^6 IU/ml culture medium preserve at 4°C; 2.2.15 cell: 2.2.15 cell line of hepatoma (Hep G2) cloned and transfected by HBV DNA, constructed by Mount Sinai Medical Center.

On page 32, please delete the paragraph beginning at line 6 and insert the following paragraph in its place:

Results from Tables 1, 2 and 3 show: After maximum innocuous concentration exponent culturing for 8 days with 2.2.15 cell, the maxima is $9.0 \pm 0 \times 10^6$ IU/ml average inhibition rate of maximum innocuous concentration rSIFN-co to HBeAg is $46.0 \pm 5.25\%$ ($P < 0.001$), IC50 is $4.54 \pm 1.32 \times 10^6$ IU/ml, SI is 3.96; rate to HBsAg is $44.8 \pm 6.6\%$, IC50 is $6.49 \pm 0.42 \times 10^6$ IU/ml, SI is 2.77. This shows that rSIFN-co can significantly inhibit the activity of HBeAg and HBsAg, but that the IFN of the contrast group and INFERGEN[®] (interferon alfacon-1) cannot. It has also been proved in clinic that rSIFN-co can decrease HBeAg and HBsAg or return them to normal levels.

Please replace pages 37-39 with the corresponding replacement sheets attached herein as Exhibit A.

Applicant(s) : Guangwen WEI, et al.
U.S. Serial No.: 10/650,365
Filed : August 28, 2003
Page : 6

Page 45, line 26:

Referring to the standard of ~~Infergen~~INFERGEN[®] (interferon
alfacon-1) for treatment of hepatitis C and according to the
ALT level and HCV-RNA test, divided the effects into three
degrees: